ATTORNEY'S DOCKET NO: 970845

U.S. DEPARTMENT OF COMMERCE, PATENT AND TRADEMARK OFFICE		DATE:
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		U.S. APPLN. NO. (if known): 08/894733
INTERNATIONAL APPLICATION NO.: PCT/IB96/01461	INTERNATIONAL FILING DATE: December 23, 1996	PRIORITY DATE CLAIMED: December 28, 1995

TITLE OF INVENTION: PARENTERAL PHARMACEUTICAL COMPOSITIONS CONTAINING AMMONIUMALKYL SALTS OF 2-ARYLPROPIONIC ACIDS

APPLICANT(S) FOR DO/EO/US: Marco GENTILE, Luigi BOLTRI and Gaetano CLAVENNA

Applicant hereby submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. _X_ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.

2. ___ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.

3. ___ This express request to begin national examination procedures (35 USC 371(f)) at any time rather than delay examination until the expiration of the time limit set in 35 USC 371(b) and PCT Articles 22 and 39(1).

4. ___ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.

5. _X_ A copy of the International Application as filed (35 U.S.C. 371(c)(2)):

   a. _X_ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. _X_ has been transmitted by the International Bureau.
   c. ___ is not required, as the application was filed in the United States Receiving Office (RO/US)

6. ___ A translation of the International Application into English (35 U.S.C. 371(c)(2)).

7. _X_ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))

   a. ___ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ___ have been transmitted by the International Bureau.
   c. ___ have not been made; however, the time limit for making such amendments has NOT expired.
   d. _X_ have not been made and will not be made.

8. ___ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).

9. _X_ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).

10. ___ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

ITEMS 11. TO 16. BELOW CONCERN OTHER DOCUMENT(S) OR INFORMATION INCLUDED:

11. ___ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.

12. _X_ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.

13. ___ A **FIRST** preliminary amendment.
    ___ A **SECOND** or **SUBSEQUENT** preliminary amendment

14. ___ A substitute specification.

15. ___ A change of power of attorney and/or address letter.

16. _X_ Other items or information: Small Entity Declaration; International Search Report.

ATTORNEY'S DOCKET NO: 970845

U.S. APPLICATION NO. (if known)	INTERNATIONAL APPLICATION NO. PCT/IB96/01461	DATE: August 27, 1997

17. _X_ The following fees are submitted:	CALCULATIONS	PTO USE ONLY
Basic National Fee (37 CFR 1.492(a)(1)-(5): Search Report has been prepared by the EPO or JPO:.....$910.00		
International preliminary examination fee paid to USPTO (37 CFR 1.482).....$700.00		
No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)).....$770.00		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO.....$1,040.00		
International preliminary examination fee (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4).....$ 94.00		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 910.00	
Surcharge of **$130.00** for furnishing the oath or declaration later than ___ 20 ____ 30 months from the earliest claimed priority date (37 DVR 1.492(e)).		

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
TOTAL	10 -20=		X $ 22.00		
INDEPENDENT	1 - 3=		X $ 80.00		
Multiple dependent claims(s) (if applicable)			+ $260.00		
TOTAL OF ABOVE CALCULATIONS =				$ 910.00	
Reduction by 1/2 for filing by small entity, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).				$ -455.00	
SUBTOTAL =				$ 455.00	
Processing fee of **$130.00** for furnishing the English translation later than ____ 20 ____ 30 months from the earliest claimed priority date (37 CFR 1.492(f)).			+		
TOTAL NATIONAL FEE =				$ 455.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). $40.00 per property +				$ 40.00	
TOTAL FEES ENCLOSED =				$ 495.00	
				Amount to be: refunded	$
				charged	$

ATTORNEY'S DOCKET NO: 970845

U.S. APPLICATION NO. (if known)	INTERNATIONAL APPLICATION NO. PCT/IB96/01461	DATE: August 27, 1997

a. _X_ A check in the amount of $495.00 to cover the above fees is enclosed. (This paper is filed in triplicate)

b. ___ Please charge my Deposit Account No. 01-2340 in the amount of $_____ to cover the above fees. (A duplicate copy of this sheet is enclosed.)

c. _X_ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 01-2340.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed to request that the application be restored to pending status.

Send All Correspondence To:

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SIGNATURE

Le-Nhung McLeland
NAME

31,541
REGISTRATION NUMBER

LNM/yap

Description

Parenteral pharmaceutical compositions containing ammoniumalkyl salts of 2-arylpropionic acids.

The object of the present invention consists of pharmaceutical compositions suitable for parenteral administration which contain alkylammonium salts of 2-arylpropionic acids.

In particular, although the parenteral pharmaceutical compositions of the invention are suitable to be obtained with any 2-arylpropionic acid having antiinflammatory activity, they preferably contain, as 2-arylpropionic acid, ketoprofen or 3-benzoyl-α-methylbenzeneacetic acid, ibuprofen or 2-(4-isobutylphenyl)propionic acid, naproxen or (S)-6-methoxy-α-methyl-naphthaleneacetic acid and tiaprofenic acid or 5-benzoyl-α-methyl-2-thiopheneacetic acid, the ketoprofen being the 2-arylpropionic acid particularly preferred.

One of the advantages represented by the pharmaceutical compositions of the invention is that it allows for the administration of the non-steroid antiinflammatory substance by a route of administration, the parenteral one, which does not show side effects as shown by the pharmaceutical forms administered by topical route such as, for example, creams, lotions, gels or ointments which, because of their easy methods of application, are widely used. It is in fact known from literature on the subject that topical administration of non-steroid anti-inflammatory drugs can, in a more or less serious manner, provoke damage to the patient's skin due to

the fotolability of the drug which, in the presence of light, undergoes a degradation process, the products of which interfere negatively on the cellular membrane by the formation of free radicals.

The pharmaceutical compositions of the invention represent, moreover, a notable improvement as far as stability and convenience of use and safety are concerned with respect to the compositions already on the market containing the same anti-inflammatory drugs.

A decisively more advantageous aspect of said pharmaceutical compositions is that their administration causes uneasiness but tolerable, with respect to the pain, sometimes intense, caused by the compositions for parenteral use on the market containing the same anti-inflammatory drugs.

In particular, as far as ketoprofen is concerned, the relative smallness of the side effects and the recognised effectiveness in the symptomatic treatment of rheumatoid arthritis, in osteoarthritis, in anchylosing spondylitis, of acute painful articular and periarticular symptoms of the musculoskeletal system, in gout and in dysmenorrhea, in the treatment of pain and inflammation which accompanies or follows orthopaedic operations, have made of such a drug one of the active principles of largest use in oral administration among anti-inflammatory non-steroid drugs of current therapeutical use.

The analgesic and anti-inflammatory effect of ketoprofen has been, in large measure, correlated to its capacity, or more specifically, to the capacity of

its S-enantiomer, of inhibiting the prostaglandin synthesis. More recently, it has been recognised that the R-enantiomer, which in human beings does not undergo an appreciable metabolic conversion in the S-antipode, has its own analgesic property, mediated by mechanism of action which, even though not fully clarified, seem to be completely independent from the prostaglandin synthesis block.

Pharmaceutical formulations for parenteral use containing as active principle ketoprofen and/or its enantiomers are thought to be particularly useful in the treatment of acute exacerbations of painful manifestations and as adjuvant in the symptomatic therapy of pain in persons suffering from terminal cancer, in individual therapeutic treatment as in association with muscle relaxants, pain-killers and central analgesics.

The 2-arylpropionic acids with anti-inflammatory activity of the present invention are made up of highly lipophilic carboxylic acids and as such are scarcely soluble in water. Nonetheless it is possible to prepare solutions of said acids, after salification in aqueous vehicles containing a surplus of a hydrate, of a bicarbonate and/or of an alkaline carbonate or an earth alkaline carbonate such as, for example, sodium hydroxide, sodium bicarbonate, of a preferably basic

α-aminoacid or of a hydroxyalkylamine, eventually in the presence of preservatives and excipients and/or dispersing agents.

Said solutions of the 2-arylpropionic acids present a

gradual instability easily evidenced from a progressive yellowing, sometimes followed by turbidity and by separation of floccules, phenomena which become more noticeable with the temperature's increase and after the solution's prolonged exposure to the light. To overcome said difficulty recourse was made to lyophilized pharmaceutical formulations from which the injectable solution is reconstituted just at the moment of use by means of solubilization in the proper solvent. These solutions contain, furthermore, variable quantities of preserving substances among which are mainly used the p-hydroxybenzoate of methyl and propyl, and supporting materials in excess such as, for example, glycine, to ensure the volume and compactness of the lyophilized substance itself. The use, together with the active principles, of a ponderal excess of supporting materials imply that the constituted solutions present pH values which vary from 6.5 to 7.3 and definitely result hypertonic. In fact, osmolarity values are measured covering an interval from 650 to 1150 mOsm/kg, which are not very compatible with the isotonicity of biological fluids which present values comprised between 275 and 295 mOsm/kg. As a result, the administration of such solutions causes pain to the patient and moreover superficial liquid effusions can come about. The presence of remarkable quantities of excipients and of the preserving agents in the solution can moreover be the cause of risks deriving from the patient's individual susceptibility to said substances.

It is known that, on the English market, formulations

have long been introduced for the extemporary use consisting of a ketoprofen solution in a mainly aqueous medium containing an excess of l-arginine, benzylic alcohol and citric acid; said solutions, which present a global pH of about 6.7 are supplied in dark glass containers for a better control of their stability.

The pharmaceutical compositions suitable for parenteral use object of the present invention, are made up of aqueous solutions of alkylammonium salt of 2-arylpropionic acids chosen from the group consisting of ketoprofen, ibuprofen, naproxen and tiaprofenic acid in racemic or in enantiomeric form, which present osmolarity values comprised in the range 270-310 mOsm/kg and pH values comprised in the range 7.0-7.5.

As alkylammonium bases are utilised bases which include alkyl radicals eventually substituted with hydroxy radicals: in the case that the alkylammonium base exists in a racemic or enantiomeric form, the salts can comprise either one or the other of said forms. Bases particularly preferred are α-aminoacids such as lysine and particularly preferred is the salt formed with the forms of said aminoacid having the natural configuration. Another preferred base is the dropropizine or 3-(4-phenyl-1-piperazinyl)-1,2-propanediols. The salifying acid is preferably employed in its racemic form even though salts formed from its separate enantiomers are comprised within the scope of the invention.

The particularly preferred salts are those of (R,S)-ketoprofen with d,l-lysine and with l-lysine

respectively described in US 4,279,926 (21.07.81) and BE 882.889 (14.05.80). Other salts, as for example the R- or S-ketoprofen salts with the separated stereoisomers of lysine and dropropizine, are also known and have been described in WO 94/20449 (15.09.94).

According to the process of the invention, the pharmaceutical compositions suitable for parenteral use containing salts of a 2-arylpropionic acid selected from the group consisting of ketoprofen, ibuprofen, naproxen and tiaprofenic acid with alkylammonium bases are prepared by solubilizing in an inert-gas atmosphere and away from light, in an aqueous solution, at a pH ranging from 7.0 and 7.5, the alkylammonium salt of the chosen 2-arylpropionic acid.

The use of an inert gas during the preparation of the solutions and their subsequent conservation allows the reaching of such a degree of stability so as to avoid a recourse to the use of preservatives and co-solvents such as, for example, alcohols or glycols for preventing the progressive yellowing of the solutions. Inert gases particularly preferred are those which are chemically inert with solvents and solutes and are compatible with the foreseen pharmaceutical use: these are, as example, nitrogen and the rare gases helium and argon and their mixtures.

Besides to grant the composition of the invention a good tolerability, the lack of benzyl alcohol or other solvent, except water for injectable preparations, also gives the consumer a precise information about

the quality of the composition itself. In fact, should the pharmaceutical composition undergo alterations due to an incorrect storage, the appearing of a characteristic whitish opalescence indicates these alterations immediately and therefore the pharmaceutical composition will be not administered.

The appearance of said opalescence representing a very sensitive index of the pharmaceutical quality of the active principle contained in the composition of the invention, is a guarantee of the quality of the composition and furthermore it represents a noticeable improvement in respect to those compositions which contain co-solvent agents, such as in particular benzyl alcohol, and consequently do not make evident the possible presence of alterations which would cause the pharmaceutical quality of the composition not anymore acceptable.

The packaging, in suitable containers of dark glass optionally disposed in a box wherein each container is separately packaged, as well as the other characteristic of the composition of the invention assures a full stability to the product as demonstrated by the tests carried out.

Moreover it has been observed that the pH adjustment of the injectable solution between 7.0 and 7.5, allows for the bringing about of, not only a useful increment of osmolarity towards that degree of hyperosmosis which better than

a slight hypo-osmosis adapts itself to a good tolerability of the injectable solution, but also an ulterior increment in the stability of the darkening solution and to the turbidity whether in tests of thermic accelerated stability or in exposure to light. For the adjustment of the pH and consequently of the osmolarity of the 2-arylpropionic acid salts, mixtures have been used of C_3-C_5 hydroxy di- and tri-carboxylic acids and the alkaline and alkaline earth salts thereof chosen in the group consisting of the tartronic, malic, tartaric and citric acids. Particularly preferred is the use of citric acid combined with the sodium hydroxy and/or sodium citrate.

The dark glass containers are preferably borosilicate phials rendered opaque to light radiations having 290 to 450 nm wave lengths.

Hereunder are given some non-limitative examples of some embodiments of the invention.

Example 1

Working sheltered from light, in an atmosphere and under bubbling nitrogen, 37.5 g (c.a.0.195M) of citric acid and 22.5 g (0.5625M) of sodium hydroxide are dissolved in 12 l of sterile water for injectable preparations, previously de-aerated. To the solution so obtained is added under stirring 1.2 kg (3M) of (R,S)-ketoprofen salt of d,l-lysine controlling the pH of the solution and eventually adjusting it to values varying from 7.0 to 7.5 with additions of sodium hydroxide.

After complete dissolution of the salt, the volume of

the solution is brought to 15 l with sterile water for injectable preparations, previously de-aerated, and stirring is continued for another 15 minutes to ensure the total homogeneity of the solution. Nitrogen is left to bubble on the solution for 15 minutes. Working is kept under pressure and in a nitrogen atmosphere, the solution is filtered through 0.22 micron cartridges, and collected in suitable shielded containers appropriately protected from exposure to the UV light radiations and then run into the machine for filling phials for distribution in 2 ml glass ampoules, which are sealed in a nitrogen atmosphere.

After sterilisation, the single phials are placed in containers which are made to hold one or more phials. If desired, the single phial holders can be protected individually by films which make them opaque to the transmission of light.

Example 2

In a similar manner, as described in the preceding Example, working is carried out by substituting the d,l-lysine salt of (R,S)-ketoprofen with the d,l-lysine salt of (R,S)-naproxen which is prepared from 0.2M of d,l-lysine dissolved in 700 ml of water to which is added, heating to the boiling point temperature, 0.202M of finely sub-divided (R,S)-naproxen. From the reaction mixture the salt separates by removing the water for distillation.

Claims

1. A pharmaceutical composition suitable for parenteral administration having anti-inflammatory and analgesic property, characterized by the fact that it contains an alkylammonium salt of a 2-arylpropionic acid selected from the group consisting of ketoprofen, ibuprofen, naproxen, tiaprofenic acid, in racemic as well as in enantiomeric form, in an aqueous solution having an osmolarity between 270 and 310 mOsm/kg and at a pH in the range between 7.0 and 7.5, said solution being free of preservatives and of supporting substances and being prepared and kept in a gas-inert atmosphere.

2. A pharmaceutical composition according to claim 1, characterized by the fact that the inert gas is nitrogen.

3. A pharmaceutical composition according to claim 1, characterized by the fact that the alkylammonium salt of the 2-arylpropionic acid is the d,l-lysine salt of (R,S)-ketoprofen and the inert gas is nitrogen.

4. A pharmaceutical composition according to claim 1, characterized by the fact that the alkylammonium salt of the 2-arylpropionic acid is the l-lysine salt of (R,S)-ketoprofen.

5. A pharmaceutical composition according to claim 1, characterized by the fact that the alkylammonium salt of the 2-arylpropionic acid is the l-lysine salt of R-ketoprofen.

6. A pharmaceutical composition according to claim 1, characterized by the fact that the alkylammonium salt of the 2-arylpropionic acid is the l-dropropizine salt

of R-ketoprofen.

7. A pharmaceutical composition according to claim 1, characterized by the fact that the alkylammonium salt of the 2-arylpropionic acid is the tromethamine salt of S-ketoprofen.

8. A pharmaceutical composition according to claim 1, characterized by the fact that the alkylammonium salt of the 2-arylpropionic acid is the tromethamine salt of R-ketoprofen.

9. A pharmaceutical composition according to claim 1, characterized by the fact that the alkylammonium salt of the 2-arylpropionic acid is the l-lysine salt of S-ketoprofen.

10. Process for the preparation of the pharmaceutical composition according to claim 1, characterized by that an alkylammonium salt of a 2-arylpropionic acid selected from the group consisting of ketoprofen, ibuprofen, naproxen and tiaprofenic acid is suitably dissolved in water for injectable preparation at a pH between 7.0 and 7.5 in an atmosphere of an inert gas and away from light.

ABSTRACT

~~Parenteral~~ pharmaceutical compositions containing ammoniumalkyl salts of 2-arylpropionic acids.

A pharmaceutical composition for parenteral administration having anti-inflammatory and analgesic properties which contain, as active principle, alkylammonium salts of 2-arylpropionic acids.

DELETED BY RO

SMALL ENTITY DECLARATION

APPLICANT OR PATENTEE DOMPE' SpA

SERIAL NO. _____ ☐ PATENT NO. _____ ATTORNEY'S DOCKET NO. _____

(Check one of blocks 1 or 2.)

1. ☐ FILED OR ISSUED _____

2. ☐ SUBMITTED HEREWITH _____

FOR Parenteral pharmaceutical compositions containing ammoniumalkyl salts of 2-arylpropionic acids
(Insert Title)

I (we) hereby declare that I (we) am (are) entitled to the benefit of small entity status with respect to the above-identified application or patent for purposes of paying reduced fees under 35 USC 41(a) & (b) to the U.S. Patent and Trademark Office.

☐ A. INDEPENDENT INVENTOR

I (we) qualify as (an) independent inventor(s) as defined in 37 CFR 1.9(c).

☐ B. INDIVIDUAL NON-INVENTOR

I would qualify as an independent inventor as defined in 37 CFR 1.9(c) if I had made the invention.

☒ C. SMALL BUSINESS CONCERN

I am ☐ THE OWNER ☐ AN OFFICIAL of the small business concern identified below and am empowered to act on behalf of the concern. The concern qualifies under 37 CFR 1.9(d) and 13 CFR 121.3-18. Rights under contract or law have been conveyed to and remain with the concern and are exclusive unless a checkmark is placed here ☐. All other rights belong to small entities as defined in 37 CFR 1.9.

☐ D. NON-PROFIT ORGANIZATION

I am an official empowered to act on behalf of the non-profit organization identified below. The organization qualifies under 37 CFR 1.9(e), sub-section: ☐ (1) ☐ (2) ☐ (3) ☐ (4). Rights under contract or law have been conveyed to and remain with the organization and are exclusive unless a checkmark is placed here ☐. All other rights belong to small entities as defined in 37 CFR 1.9.

I (we) acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b)).

I (we) declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

A. INDEPENDENT INVENTOR(S) B. INDIVIDUAL NON-INVENTOR(S)

Name	Signature	Date

C. BUSINESS CONCERN D. NON-PROFIT ORGANIZATION

DOMPE' SpA — Name of Concern or Organization

Via Campo Di Pile - 67100 L'Aquila Italy — Address

By Sergio DOMPE' — Name of Person Signing

Signature

Managing Director — Title

11th July 1997 — Date

Rev. #1. March 1991

Please direct all communications to the following address: ARMSTRONG, WESTERMAN, HATTORI, McLELAND & NAUGHTON
1725 K Street, N.W., Suite 1000
Washington, D.C. 20006
Telephone: (202) 659-2930 Fax: (202) 887-0357

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Title 18 of the United States Code, § 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

1-D Full name of sole or first inventor (given name, family name) Marco GENTILE

(See note C above) Inventor's Signature _____ Date 11th July 1997

Residence L'Aquila Italy ITX Citizenship Italian

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2-D Full name of second inventor (given name, family name) Luigi BOLTRI

Inventor's Signature _____ Date 11th July 1997

Residence L'Aquila Italy ITX Citizenship Italian

Post Office Address Via Campo Di Pile - 67100 L'Aquila - Italy

3-D Full name of third inventor (given name, family name) Gaetano CLAVENNA

Inventor's Signature _____ Date 11th July 1997

Residence Milano Italy ITX Citizenship Italian

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Full name of fourth inventor (given name, family name) _____

Inventor's Signature _____ Date _____

Residence _____ Citizenship _____

Post Office Address _____

Full name of fifth inventor (given name, family name) _____

Inventor's Signature _____ Date _____

Residence _____ Citizenship _____

Post Office Address _____

Full name of sixth inventor (given name, family name) _____

Inventor's Signature _____ Date _____

Residence _____ Citizenship _____

Post Office Address _____

Full name of seventh inventor (given name, family name) _____

Inventor's Signature _____ Date _____

Residence _____ Citizenship _____

Post Office Address _____

Full name of eighth inventor (given name, family name) _____

Inventor's Signature _____ Date _____

Residence _____ Citizenship _____

Post Office Address _____

A, W, H, McL & N Docket No._____ ARMSTRONG, WESTERMAN, HATTORI, McLELAND & NAUGHTON

Declaration For U.S. Patent Application

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention **entitled**
(Insert Title) Parenteral pharmaceutical compositions containing ammoniumalkyl salts of 2-arylpropionic acids.
the specification of which is attached hereto unless the following is checked:

[X] was filed on December 23rd, 1996 as United States Application Number or PCT International Application Number PCT/IB96/01461 and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claim(s), as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, § 119 (a) - (d) of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

(List prior foreign applications. See note A on back of this page)	(Number)	(Country)	(Day/Month/Year Filed)	Priority Claimed
	MI95A 002777	Italy	28 December 1995	☒ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No

(See note B on back of this page) ☐ See attached list for additional prior foreign applications

I hereby claim the benefit under Title 35, United States Code, § 119(e) of any United States provisional application(s) listed below.

(Application Number)	(Filing Date)

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of the application:

(List Prior U.S. Applications)	(Application Serial Number)	(Filing Date)	(Status) (patented, pending, abandoned)

I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

James E. Armstrong, III, Reg. No. 18,366; William F. Westerman, Reg. No. 29,988; Ken-Ichi Hattori, Reg. No. 32,861; Le-Nhung McLeland, Reg. No. 31,541; Ronald F. Naughton, Reg. No. 24,616; John R. Pegan, Reg. No. 18,069; William G. Kratz, Jr., Reg. No. 22,631; Albert Tockman, Reg. No. 19,722; Mel R. Quintos, Reg. No. 31,898; Donald W. Hanson, Reg. No. 27,133; Stephen G. Adrian, Reg. No. 32,878; William L. Brooks, Reg. No. 34,129; John F. Carney, Reg. No. 20,276; Edward F. Welsh, Reg. No. 22,455; Patrick D. Muir, Reg. No. 37,403; Gay A. Spahn, Reg. No. 34,978; and John P. Kong, Reg. No. 40,054

NOTES

A. Please list all foreign applications relating to the invention and check block "yes" or "no".

B. If more than 4 prior foreign applications, please check this box and attach a sheet listing the remaining prior foreign applications.

C. For residence in the U.S., indicate city and state, for residence outside the U.S., indicate city and country. The "Post Office Address" must be an address acceptable by a Post Office for delivery of mail.